Communications to the Editor

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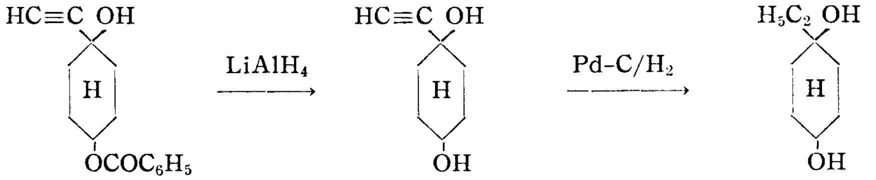
Studies on the Chemical Structure of Monohydroxy Derivative of 1-Ethynylcyclohexyl Carbamate

In a previous work,[1] the author isolated one of metabolites of 1-ethynylcyclohexyl carbamate (ECC) from human urine and its chemical structure was confirmed as OH-ECC, but the position of this hydroxyl group was not determined.

Recently, McMahon[2] reported that the position of the hydroxyl group in OH-ECC was in the position *para* to the ethynyl group. In his case, the metabolite was reduced, then hydrolyzed, and 1-ethylcyclohexanediol thereby obtained was confirmed as 1-ethylcyclohexane-1,4-diol by comparison with a synthetic sample.

In the present case, OH-ECC was hydrolyzed with NaOH and 1-ethynylcyclohexane-1,4-diol was obtained directly as crystals. A solution of 200 mg. of OH-ECC dissolved in 22 cc. of 0.1*N* NaOH solution was heated for 4.5 hr. in a boiling bath, the reaction mixture was neutralized with 5% HCl, and evaporated to dryness in a reduced pressure. The residue was extracted with Et_2O, the extract was evaporated to dryness, and white crystalline solid was obtained; yield, 119 mg. The white crystals were dissolved in Et_2O and chromatographically fractionated through alumina column. The chromatogram was first eluted with CH_2Cl_2-benzene (1:1) and the solvent was evaporated from the effluent, leaving a minute amount of crystals, which melted from 71° to 89°, but further purification was unsuccessful. The chromatogram was next eluted with benzene-EtOH (4:1), the solvent was evaporated from the effluent, and the residue was recrystallized from benzene to 66 mg. of white needles, m.p. 98∼99° (*Anal.* Calcd. for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found : C, 68.70; H, 8.36).

Jones and Sondheimer[3] reported the preparation of 1-ethynyl-4-benzoxycyclohexanol (I) and its conversion to 1-ethynylcyclohexane-1,4-diol (Ⅱ). Further, McMahon separated (Ⅱ) into two kinds of isomers (Ⅱa and Ⅱb), and prepared two isomers of 1-ethylcyclohexane-1,4-diol (Ⅲa and Ⅲb) by reducing each of them.



(I) (Ⅱa) m.p. 144∼145° (Ⅲa) m.p. 107∼109°
(Ⅱb) m.p. 96∼98° (Ⅲb) m.p. 113∼114°

The product of m.p. 98∼99°, which was obtained directly from OH-ECC, agreed well with (Ⅱb) in its melting point. Further confirmation was attempted by reduction. A solution of 20 mg. of this product dissolved in 15 cc. of MeOH, added with 50 mg. of prereduced Pd-$CaCO_3$, was shaken in H_2 stream. After reduction was over, the catalyst was filtered off and the filtrate was evaporated to dryness. The residue was recrystallized from benzene, m.p. 113∼113.5° (*Anal.* Calcd. for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found : C, 66.29; H, 10.88).

These results strongly support the chemical structure of OH-ECC suggested by McMahon, that the hydroxyl group is in the position *para* to the ethynyl group.

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[1] T. Murata : This Bulletin, **8**, 629 (1960).
[2] R. E. McMahon : J. Org. Chem., **24**, 1834 (1959).
[3] E. R. H. Jones, F. Sondheimer : J. Chem. Soc., **1949**, 615.